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L3 ANSWER 2 OF 49 MEDLINE DUPLICATE 1
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TITLE: **Rapamycin** impairs antigen uptake of human
dendritic cells.
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AB BACKGROUND: **Rapamycin** is a recently introduced immunosuppressive
agent. Its effect on lymphocytes has been extensively studied. Whether it
can also modulate **dendritic** cell (DC) function is unknown.
METHODS: The effect of **rapamycin** on differentiation, antigen
uptake, and the immunostimulatory capacity of human DC was examined. DC
were derived from monocytes upon culture with interleukin (IL)-4 and
granulocyte-macrophage colony-stimulating factor in the presence or
absence of **rapamycin** (0.1-100 ng/mL). Surface phenotype and
antigen uptake capacity of DC were assessed by flow cytometry.
Immunostimulatory capacity was measured by mixed lymphocyte culture.
RESULTS: **Rapamycin** reduced DC recovery and increased DC
apoptosis. DC differentiated in the presence of **rapamycin**
(rapa-DC) had increased expression of CD1a, CD1b, and CD1c and decreased
expression of MHC I, MHC II, CD80, CD86, and CD40. Antigen uptake
receptor
expression (mannose receptor, CD32, CD91, CD46) was decreased, and
receptor-mediated endocytosis of fluorescein isothiocyanate-dextran was
markedly impaired in rapa-DC, as were fluid phase endocytosis of Lucifer
Yellow and phagocytic activity of bacteria and dead or apoptotic cells.
CD40 ligand-induced production of both IL-12 and IL-10 was reduced in
rapa-DC, and allogeneic T lymphocyte responses were moderately impaired
when rapa-DC were used as stimulator cells. Neither cyclosporine nor
FK506
affected DC function. However, the effects of **rapamycin** on DC
could be completely inhibited by a 10-fold excess of FK506 but not by up
to 100-fold excess of cyclosporine. CONCLUSION: **Rapamycin** has a
unique and profound inhibitory effect on DC function, which seems to be
at
least in part mediated by the FKBP immunophilins.